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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/807,961	03/24/2004	Richard A. Gross	14690.010USA	4091

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EXAMINER

OLSON, ERIC

ART UNIT PAPER NUMBER

1623

DATE MAILED: 11/07/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>	
	10/807,961	GROSS, RICHARD A.	
	<b>Examiner</b>	<b>Art Unit</b>	
	Eric S. Olson	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) ☒ Responsive to communication(s) filed on 28 August 2006.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) ☒ Claim(s) 1-35 is/are pending in the application.
- 4a) Of the above claim(s) 27-33 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-26, 34 and 35 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 24 March 2004 and 28 June 2004 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                       | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)   | Paper No(s)/Mail Date. _____                                      |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>March 24, 2004</u> .  | 6) <input type="checkbox"/> Other: _____                          |

**Detailed Action**

This application claims benefit of provisional application 60/457070, filed March 24, 2003.

***Election/Restrictions***

Applicant's election without traverse of group I, drawn to a method of treating septic shock, filed August 26, 2006, is acknowledged.

Claims 27-33 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on August 26, 2006.

Claims 1-26, 33, and 34 are pending in this application and examined on the merits herein.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 33 and 34 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: any steps involving the application of the claimed sophorolipids to form a natural fermentation mixture, or to treat sepsis and septic shock.

Claims 8-17 recites the limitation "wherein the sophorolipid is ..." There is insufficient antecedent basis for this limitation in the claim.

The independent claims do not recite any specific sophorolipid but rather a crude mixture of sophorolipids produced by fermentation. As this mixture contains multiple sophorolipids, the term, "the sophorolipid" in the dependent claims lacks antecedent basis. Furthermore, claim 6 recites a step of specifically isolating and utilizing the lactonic fraction of the crude sophorolipid mixture. Dependent claim 15 recites the limitation, "wherein the 17-L-[(2'-O- $\beta$ -D-glucopyranosyl- $\beta$ -D-glucopyranosyl)-oxy]-cis-9-octadecanoate based sophorolipid is selected from the group consisting of 17-L-[(2'-O- $\beta$ -D-glucopyranosyl- $\beta$ -D-glucopyranosyl)-oxy]-cis-9-octadecanoate-6',6''-diacetate, hexyl 17-L-[(2'-O- $\beta$ -D-glucopyranosyl- $\beta$ -D-glucopyranosyl)-oxy]-cis-9-octadecanoate, and ethyl 17-L-[(2'-O- $\beta$ -D-glucopyranosyl- $\beta$ -D-glucopyranosyl)-oxy]-cis-9-octadecanoate."

These species are not lactonic, and thus lack antecedent basis in the base claim 6.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-26, 33, and 34 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods comprising a treatment for septic shock and sepsis, does not reasonably provide enablement for prophylaxis of

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septic shock and sepsis. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The Applicant's attention is drawn to *In re Wands*, 8 USPQ2d 1400 (CAFC1988) at 1404 where the court set forth eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApl's 1986) at 547 the court recited eight factors:

(1) The nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

Nature of the invention: The claimed invention is drawn to a therapeutic method for treatment or prophylaxis of a disorder.

The state of the prior art: Sphorolipids are known in the art to be obtainable by microbial fermentation and to have certain antimicrobial properties. They are not known to be useful for the long-term prevention or prophylaxis of septic shock or any other disorders.

In general, preventing an acute disorder such as septic shock would require that the treatment be effective if administered at any time prior to the onset of septic shock. This requires either that the compound remain in the subject's system for an extended period of time, (which is unlikely and undesirable) or that it trigger a permanent change

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in the subject's body so as to render the subject immune to a particular disorder, as is the case with a vaccine.

It should also be noted that, for the purpose of claim interpretation, references to "prevention" or "prophylaxis" in the art are not considered relevant to interpretation of prevention in the claims unless Applicant's disclosure explicitly defines the term prophylaxis in the claims to mean a clinical outcome short of absolute perfection.

The relative skill of those in the art: The relative skill of those in the art is high.

The predictability or unpredictability of the art: Prophylaxis a disorder is not the same as treatment of said disorder. In order to prevent a disorder, as opposed to merely delaying or reducing its symptoms, a treatment must either render the subject completely resistant to said disorder after a single treatment or a limited number of treatments, or else, when continued indefinitely, continue to completely suppress the occurrence of said disorder. In order to practice a preventative method, one of skill in the art must know the answer to several questions in addition to the effectiveness of the therapy in short-term relief of symptoms, including:

1) What is the duration of a single course of therapy? How often must the therapy be administered to completely suppress the disease?

2) Does the subject develop tolerance to the therapy over time? Does the disease eventually progress to a point where the therapy is unable to completely suppress all symptoms? For example, will a metastatic cancer eventually adapt to overcome treatments directed to preventing it from metastasizing into the bone? Or will a case of osteoporosis or rheumatoid arthritis ultimately progress to a point where

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symptoms develop regardless of which therapy is administered. Or in the case of septic shock, will the patient encounter a strain of bacteria which produce a case of septic shock which cannot be treated or prevented by the claimed therapy?

3) What are the long-term effects of the therapy? Does it cause progressive damage to the kidneys, liver, or other organs? Does the active agent accumulate in the subject's tissues? Is the minimum dose necessary to completely prevent the disease safe for long-term administration? Are there any steps that can be taken to reduce side effects?

For this reason, many therapies which are suitable for short-term relief of symptoms are not suitable for lifelong prevention of disease. For example, antibiotics, chemotherapeutics, and antiviral drugs are not normally administered to healthy subjects in order to prevent the development of infection or cancer.

The Breadth of the claims: In the absence of an explicit definition in Applicant's specification, "prophylaxis" as recited in the instant claims, is interpreted to mean the complete and total blocking of all symptoms of a disorder for an indefinite period of time. Any therapy which merely reduces the number or severity of symptoms, or which is effective for a period shorter than the subject's remaining lifespan, is considered to be ineffective at preventing a disorder.

The amount of direction or guidance presented: No guidance is given in the specification suggesting any reason to believe that administration of a sophorolipid mixture is totally effective against all present and future occurrences of sepsis or septic shock. In fact, according to table 2, p. 11 in Applicant's specification, sophorolipids are

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ineffective in reducing mortality from septic shock when administered before or simultaneously with lipopolysaccharide. Therefore, based on Applicant's data, it is highly unlikely that sophorolipids are capable of preventing septic shock when administered before the onset of bacteremia.

The presence or absence of working examples: No working examples are given demonstrating the successful prophylaxis of sepsis or septic shock.

Note that lack of working examples is a critical factor to be considered, especially in a case involving an unpredictable and undeveloped art such as the prevention of disease. See MPEP 2164.

The quantity of experimentation necessary: As mentioned above, the short-term usefulness of a therapy for treatment of an acute disorder is no guarantee of its long-term usefulness for prophylaxis. Because no guidance is given for the use of the claimed therapeutic method for the long-term prevention of disease, one skilled in the art wishing to practice the invention would be unable to do so without first gathering information as to the long-term effectiveness of the therapy. In particular, one skilled in the art, in order to practice the invention for prevention of disease, would need to know whether the preventative effect remains potent over the long term.

In order to answer these questions in the absence of any existing data, one skilled in the art, in order to practice the invention, would undertake long-term animal tests, preferably over a period of years, preferably involving a relatively long-lived experimental animal such as dogs or monkeys, or a human clinical trial. Animal experiments include, along with induction of the disease state, administration of the

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potential pharmaceutical compound and collection and analysis of data, additional burdens associated with compliance with animal welfare regulations, care, feeding, and other maintenance of the animals, dissection of dead animals to collect data, and disposal of dead animals after the protocol is finished. Administering the claimed compounds for a period of years to a suitable subject population is an undue amount of experimentation needed in order to practice the full range of the claimed invention. As prophylaxis in the full sense is an extremely high bar for any clinical outcome, there is no reason to believe that the therapy would be successful, and any actual success would be a surprising and unpredictable result.

*Genentech*, 108 F.3d at 1366, states that, "a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion." And "patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable."

Therefore, in view of the Wands factors, as discussed above, particularly the unpredictability of the art and the lack of guidance, Applicants fail to provide information sufficient to practice the claimed invention for the prophylaxis of sepsis and septic shock.

### ***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

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(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 34 is rejected under 35 U.S.C. 102(b) as being anticipated by Davila et al.

(Reference cited by Applicant in PTO-1449) Davila et al. discloses a method of producing sophrolipids by fermentation of *Candida bombicola* CBS 6009. (p. 140, left column, second paragraph) This mixture includes various lactones and free acids, including the acid 6'-6''-diacetate. (Table 1, p. 142, right column, top, and figure 5, p. 148 bottom) Therefore this process is reasonably considered to be an application of sophrolipids synthesized by *Candida bombicola* in a fermentation mixture to form a natural mixture of lactonic sophrolipids and non-lactonic sophrolipids in combination with at least one sophrolipid selected from:

a) sophrolipids synthesized by *Candida bombicola* in a fermentation mixture to form a natural mixture of lactonic sophrolipids and non-lactonic sophrolipids, or

b) 17-L-[(2'-O- $\beta$ -D-glucopyranosyl- $\beta$ -D-glucopyranosyl)-oxy]-cis-9-octadecanoate-6',6''-diacetate, or

e) combinations thereof.

Therefore Davila et al. anticipates instant claim 34.

### Conclusion

No claims are allowed in this application.

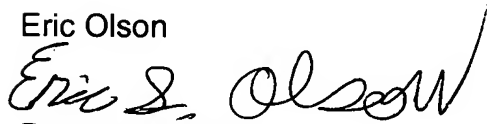
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Eric S. Olson whose telephone number is 571-272-9051. The examiner can normally be reached on Monday-Friday, 8:30-5:00.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shaojia Anna Jiang can be reached on (571)272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Eric Olson



Patent Examiner

AU 1623

11/2/06

Anna Jiang



Supervisory Patent Examiner

AU 1623